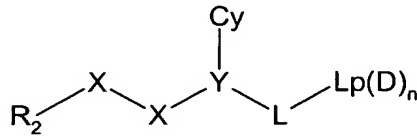


Clean Set of Claims

1. A serine protease inhibitor compound of formula (I)



5

(I)

wherein:

R₂ is a 5 or 6 membered aromatic carbon ring optionally interrupted by a nitrogen, oxygen or sulphur ring atom, optionally being substituted in the 3 and/or 4 position (in relation to the point of attachment of X-X) by halo, nitro, thiol, haloalkoxy, hydrazido, alkylhydrazido, amino, cyano, haloalkyl, alkylthio, alkenyl, alkynyl, acylamino, tri or difluoromethoxy, carboxy, acyloxy, MeSO₂- or R₁, or the substituents at the 3 and 4 positions taken together form a fused ring which is a 5 or 6 membered carbocyclic or heterocyclic ring optionally substituted by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or R_{1j}, and optionally substituted in the position alpha to the X-X group (i.e. 6 position for a six membered aromatic ring etc) by amino, hydroxy, halo, alkyl, carboxy, alkoxy, carbonyl, cyano, amido, aminoalkyl, alkoxy or alkylthio with the proviso that R₂ cannot be aminoisoquinolyl;

each X independently is a C, N, O or S atom or a CO, CR_{1a}, C(R_{1a})₂ or NR_{1a} group, at least one X being C, CO, CR_{1a} or C(R_{1a})₂;

each R_{1a} independently represents hydrogen or hydroxyl, alkoxy, alkyl, aminoalkyl, hydroxyalkyl, alkoxyalkyl, alkoxy, carbonyl, alkylaminocarbonyl, alkoxy, carbonyl, amino, acyloxymethoxycarbonyl or alkylamino optionally substituted by hydroxy, alkylamino, alkoxy, oxo, aryl or cycloalkyl;

R₁ is as defined for R_{1a}, provided that R₁ is not unsubstituted aminoalkyl;

Y (the α-atom) is a nitrogen atom or a CR_{1b} group;

Cy is a saturated or unsaturated, mono or poly cyclic, homo or heterocyclic group, optionally substituted by groups

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~~R_{3a} or R_{3i}X_i;~~

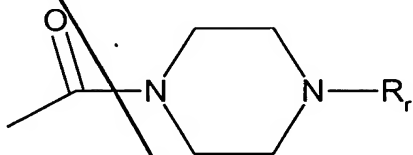
~~each R_{3a} independently is R_{1c}, amino, halo, cyano, nitro, thiol, alkylthio, alkylsulphonyl, alkylsulphenyl, triazolyl, imidazolyl, tetrazolyl, hydrazido, alkylimidazolyl, thiazolyl, alkylthiazolyl, alkylloxazolyl, oxazolyl, alkylsulphonamido, alkylaminosulphonyl, aminosulphonyl, haloalkoxy, haloalkyl, a group of the formula -C(X³)N(R¹¹)R¹² (wherein X³ is O or S; and R¹¹ and R¹² are independently selected from hydrogen, methyl or ethyl or together with the nitrogen atom to which they are attached form a pyrrolidin-1-yl, piperidin-1-yl or morpholino group), or -OCH₂O- which is bonded to two adjacent ring atoms in Cy;~~

~~X_i is a bond, O, NH or CH₂;~~

~~R_{3i} is phenyl, pyridyl or pyrimidinyl optionally substituted by R_{3a};~~

~~R_{1b}, R_{1c} and R_{1j} are as defined for R_{1a}; and~~

~~-L-Lp(D)_n is of the formula:~~



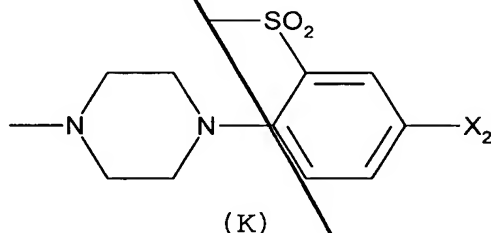
~~in which R_f is -(CH₂)_c-R_c, -CHR_eR_f, -CH₂-CHR_eR_f, -CH₂-CH₂-CHR_eR_f, or R_g in which c is 1 or 2; R_c is thienyl, thiazolyl (which may bear an amino substituent), isothiazolyl, oxazolyl, isoxazolyl, pyrazolyl, imidazolyl, pyridyl (which may bear an alkylsulphonyl, aminosulphonyl, alkylaminosulphonyl, alkylaminocarbonyl, amino, amido, (1-4C)alkoxycarbonyl, carboxy, acetyl amino, chloro, fluoro, cyano, (1-3C)alkyl, trifluoromethyl, methoxy, ethoxy, nitro, hydroxy, alkylsulphonylamino, triazolyl or tetrazolyl substituent), pyrimidinyl, pyridazinyl, pyrazinyl or phenyl (which may bear a methyl, methylamino, dimethylamino, carboxy, dialkylaminosulphonyl, alkylsulphonyl, aminosulphonyl, alkylaminosulphonyl, alkylaminocarbonyl, amino, amido, alkoxycarbonyl, acetyl amino, chloro, fluoro, cyano, methoxy, ethoxy, nitro, hydroxy, alkylsulphonylamino, triazolyl or tetrazolyl substituent); each of R_e and R_f independently is hydrogen or C₁₋₃alkyl; or CHR_eR_f is cyclopentyl (which may~~

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bear a hydroxy, amino, (1-3C)alkoxy, (1-3C)hydroxyalkyl, (1-3C)alkyl, carboxy, methoxycarbonyl or ethoxycarbonyl substituent at the 3- or 4-position), cyclohexyl (which may bear a hydroxy, amino, (1-3C)alkoxy, (1-3C)hydroxyalkyl, (1-3C)alkyl, carboxy, methoxycarbonyl or ethoxycarbonyl substituent at the 3- or 4-position), tetrahydropyran-4-yl, tetrahydrothiopyran-4-yl, pyrrolidin-3-yl (which may bear a hydroxy, amino, (1-3C)alkoxy, (1-3C)hydroxyalkyl, (1-3C)alkyl, carboxy, methoxycarbonyl or ethoxycarbonyl substituent at the 1-position), piperidin-4-yl (which may bear a hydroxy, amino, (1-3C)alkoxy, (1-3C)hydroxyalkyl, (1-3C)alkyl, carboxy, methoxycarbonyl or ethoxycarbonyl substituent at the 1-position), or indan-2-yl; and R_g is 2-methylsulphonylphenyl which may bear a 4-fluoro substituent or R_g is λ^6 -1,1-dioxobenzo[b]thiophen-7-yl;

or a physiologically-tolerable salt thereof; provided that $Lp(D)_n$ is not of the formula (K):



wherein X_2 is fluoro or hydrogen.

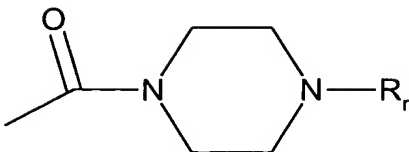
2. (amended) A compound according to claim 1 wherein

25 Cy is a saturated or unsaturated, mono or poly cyclic, homo or heterocyclic group, optionally substituted by groups R_{3a} or phenyl optionally substituted by R_{3a} ;

each R_{3a} independently is R_{1c} , amino, halo, cyano, nitro, thiol, alkylthio, alkylsulphonyl, alkylsulphenyl, triazolyl, imidazolyl, tetrazolyl, hydrazido, alkyl imidazolyl, thiazolyl, alkyl thiazolyl, alkyl oxazolyl, oxazolyl, alkylsulphonamido, alkylaminosulphonyl, aminosulphonyl, haloalkoxy and haloalkyl; and

-L- $Lp(D)_n$ is of the formula:

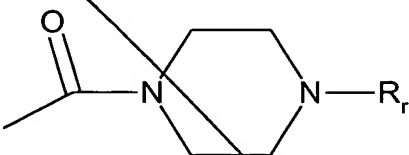
- 4 -



in which R_f is $-(CH_2)_c-R_c$, $-CHReR_f$, $-CH_2-CHReR_f$, or R_g in which c is 1 or 2; R_c is pyridyl or phenyl (which phenyl may bear a fluoro, chloro, methyl, $CONH_2$, SO_2NH_2 ,

- 5 methylaminosulphonyl, dimethylaminosulphonyl, methoxy or methylsulphonyl substituent); each of R_e and R_f independently is hydrogen or C_{1-3} alkyl; or $CHReR_f$ is cyclopentyl (which may bear a methyl, ethyl or hydroxymethyl substituent at the 3- or 4-position), cyclohexyl (which may bear a methyl, ethyl or
- 10 hydroxymethyl, (1-3C)alkyl, carboxy, methoxycarbonyl or ethoxycarbonyl substituent at the 3- or 4-position), tetrahydropyran-4-yl, tetrahydrothiopyran-4-yl, pyrrolidin-3-yl (which may bear a 1-methyl substituent), piperidin-4-yl (which may bear a 1-methyl substituent), or indan-2-yl; and R_g
- 15 is 2-methylsulphonylphenyl which may bear a 4-fluoro substituent or R_g is λ^6 -1,1-dioxobenzo[b]thiophen-7-yl.

3. A compound according to claim 1 wherein $-L-Lp(D)_n$ is of the formula:



- 20 in which R_f is $-(CH_2)_c-R_c$; in which c is 2; R_c is thienyl, thiazolyl (which may bear an amino substituent), isothiazolyl, oxazolyl, isoxazolyl, pyrazolyl, imidazolyl, pyridyl (which may bear an amino, methoxycarbonyl, carboxy,
- 25 fluoro, cyano, methyl, methylsulphonyl, aminosulphonyl, methylaminosulfonyl, dimethylaminosulfonyl, or trifluoromethyl substituent), pyrimidinyl, pyridazinyl, pyrazinyl or phenyl (which phenyl may bear a fluoro, chloro, cyano, methyl, amino, methylsulphonyl, aminosulphonyl, methylaminosulphonyl,
- 30 dimethylaminosulphonyl, methylamino, dimethylamino, carboxy, methoxycarbonyl or methoxy substituent).

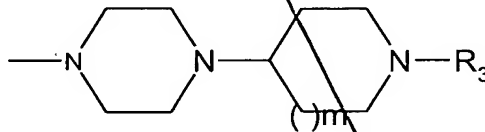
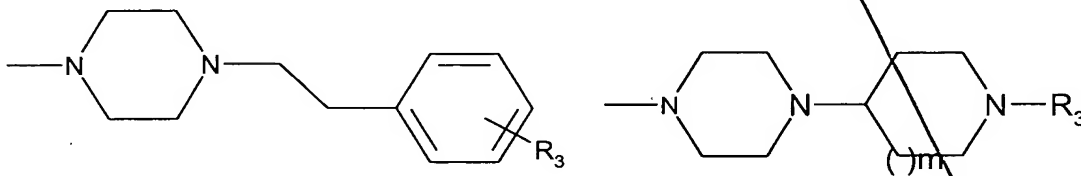
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4. (amended) A compound according to claim 3 wherein R_c is thiazolyl (which may bear an amino substituent), pyrimidinyl, pyrazolyl, imidazolyl, pyridyl (which may bear a methylsulphonyl, aminosulphonyl, methylaminosulfonyl, dimethylaminosulfonyl, fluoro, cyano, methyl or trifluoromethyl substituent), pyridazinyl, pyrazinyl or phenyl (which phenyl may bear a fluoro, chloro, cyano, methyl, amino, methylamino, dimethylamino, carboxy, methoxycarbonyl, methylsulphonyl, aminosulphonyl, methylaminosulfonyl, dimethylaminosulfonyl, or methoxy substituent).

5. (amended) A compound according to claim 4 wherein R_c is thiazolyl (which may bear an amino substituent), pyrazolyl, imidazolyl, pyridyl (which may bear a fluoro, cyano, methyl or trifluoromethyl substituent), pyridazinyl or pyrazinyl.

6. (amended) A compound according to claim 5 wherein R_c is thiazol-2-yl, 2-aminothiazol-4-yl, pyrazol-1-yl, pyrazol-4-yl, pyridazin-3-yl, imidazol-1-yl, imidazol-4-yl, pyrazin-2-yl, pyrid-2-yl, pyrid-3-yl, pyrid-4-yl, 3-fluoropyrid-4-yl, 2-cyanopyrid-4-yl, 2-methylpyrid-4-yl or 2-trifluoromethylpyrid-6-yl.

7. (amended) A compound according to claim 1 wherein L is CO and -Lp(D)_n is of the formula:



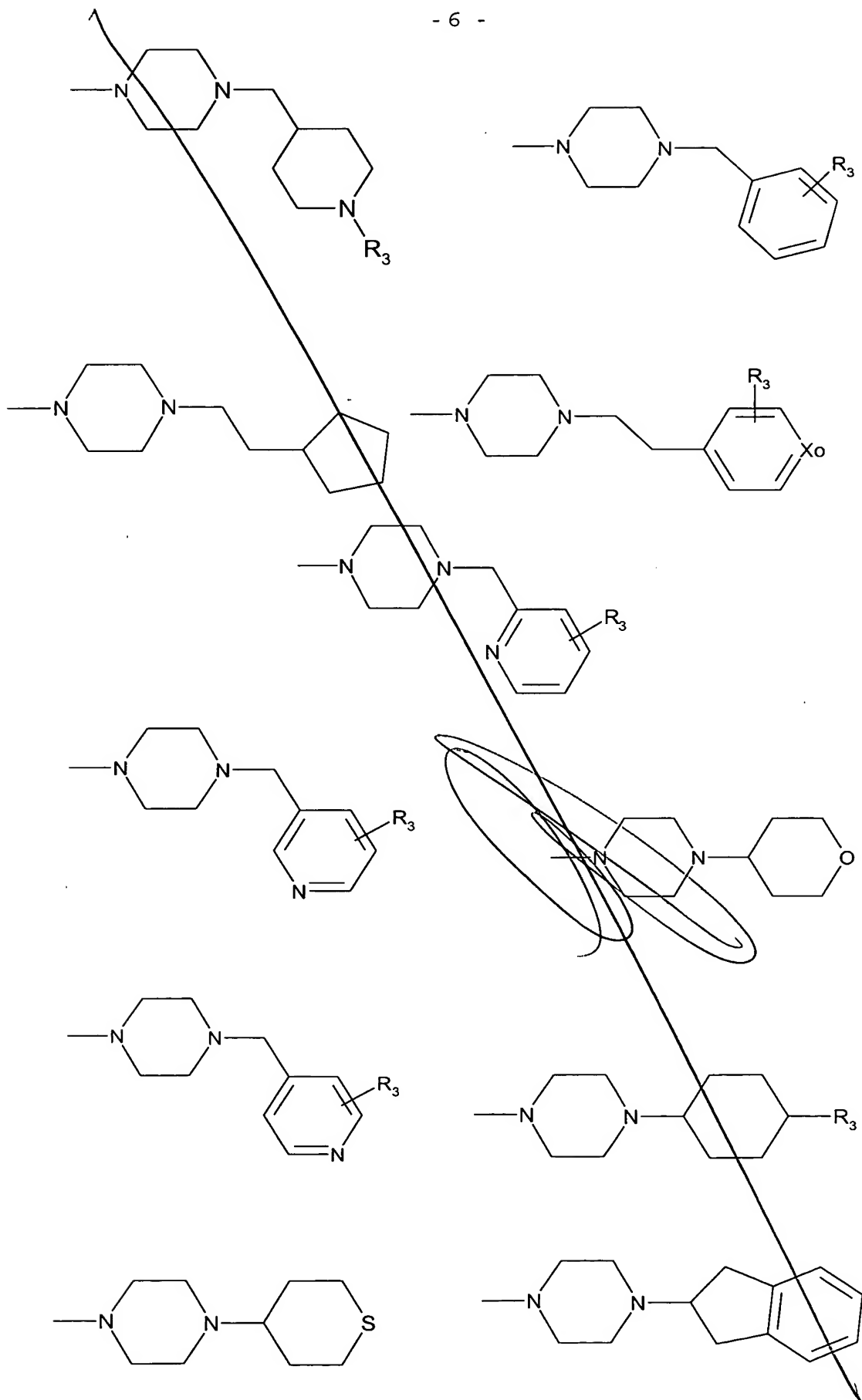
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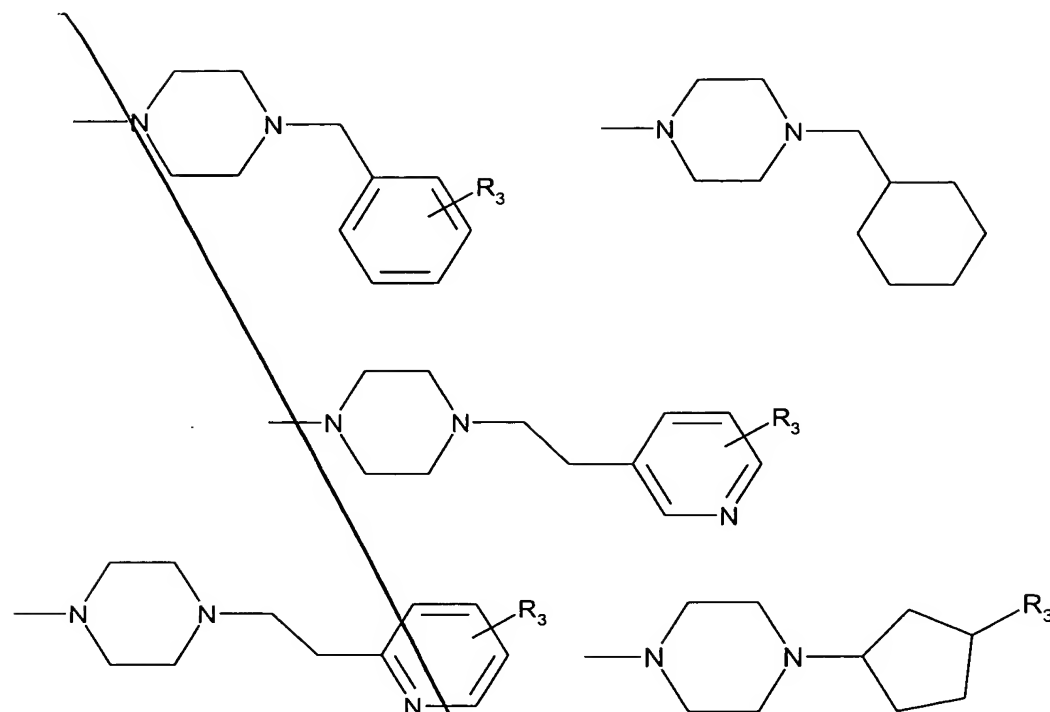
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wherein;

m represents 0 or 1;

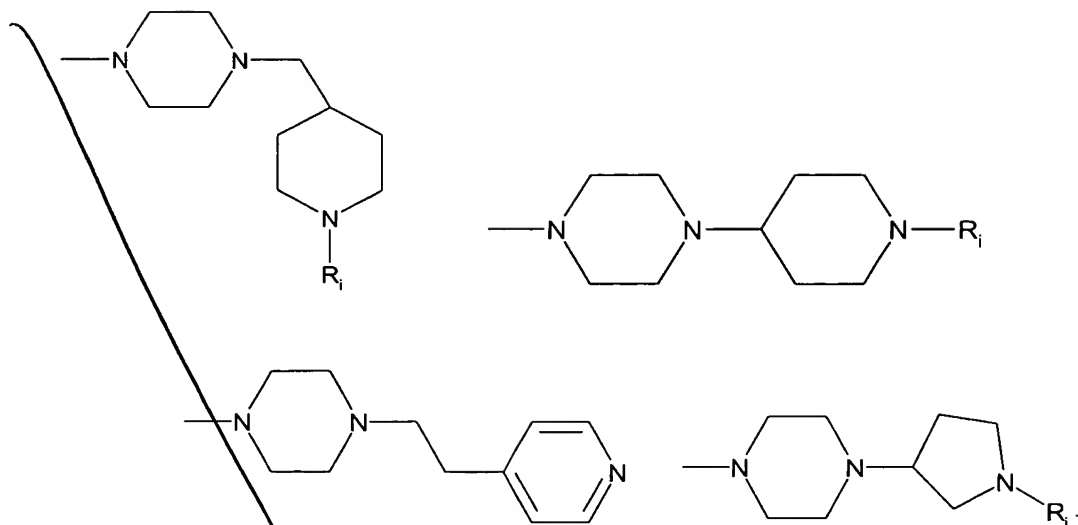
X⁰ represents CH or N; and

when R₃ is present as a substituent on an aromatic ring, it is selected from hydrogen, alkylsulphonyl, aminosulphonyl, alkylaminosulphonyl, alkylaminocarbonyl, amino, amido, alkoxy, carbonyl, acetyl, amino, chloro, fluoro, cyano, methoxy, ethoxy, nitro, hydroxy, alkylsulphonylamino, triazolyl and tetrazolyl; and

when R₃ is present as a substituent on a saturated ring, it is selected from hydrogen, hydroxy, amino, (1-3C)alkoxy, (1-3C)hydroxyalkyl, (1-3C)alkyl, carboxy, methoxycarbonyl and ethoxycarbonyl.

8. A compound according to claim 7 wherein -Lp(D)_n is of the formula:

- 8 -



wherein R_1 is hydrogen or (1-6C)alkyl.

5

9. (amended) A compound according to claim 1 wherein R_2 is phenyl, thien-2-yl, naphthyl, indol-2-yl, indol-6-yl, benzo[b]furan-5-yl, benzo[b]thiophen-2-yl or benzimidazol-2-yl (each of which is optionally substituted as defined in claim 1).

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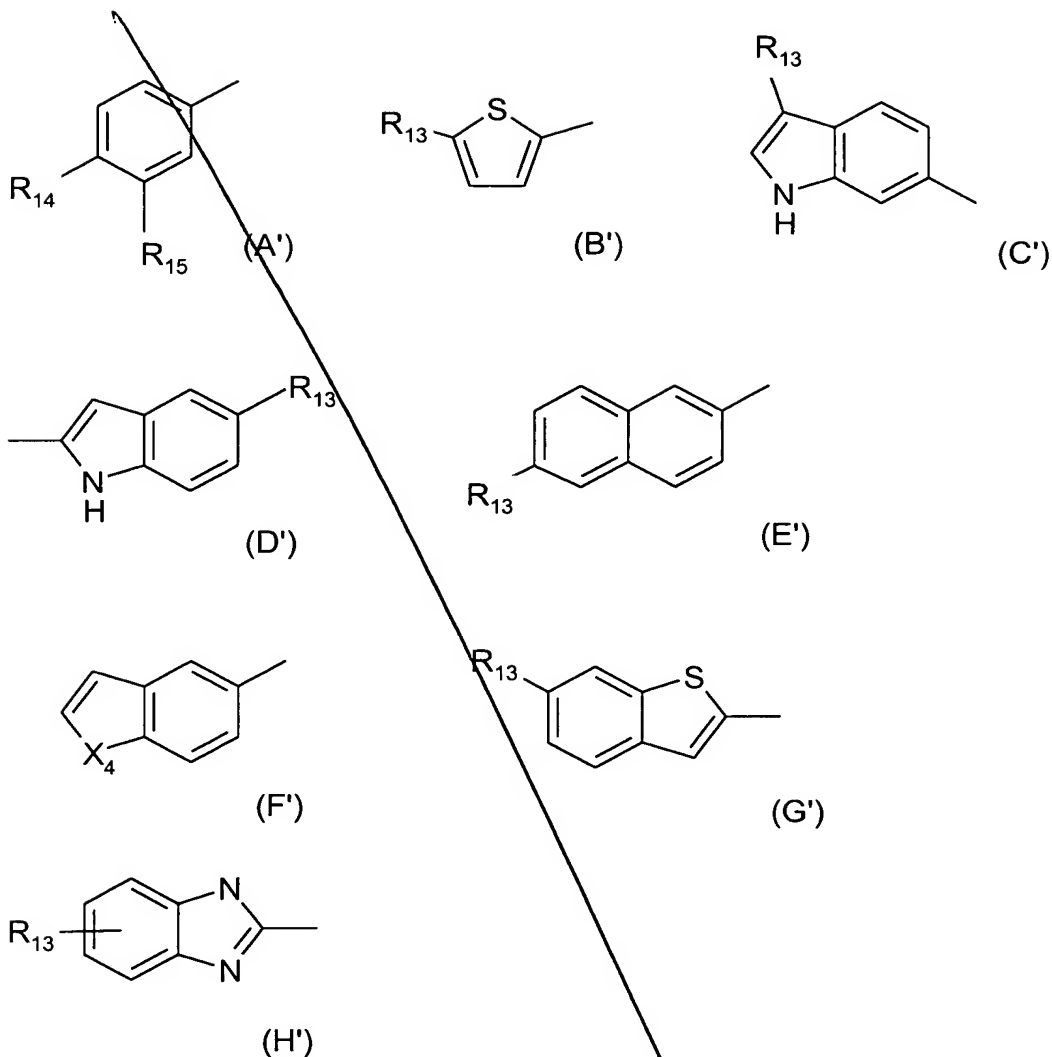
10. (amended) A compound according to claim 9 wherein optional substituents for R_2 are selected from:

fluoro, chloro, bromo, iodo, nitro, thiol, difluoromethoxy, trifluoromethoxy, hydrazido, methylhydrazido, amino, cyano, trifluoromethyl, methylthio, vinyl, ethynyl, acetylamino, carboxy, acetoxy, hydroxy, methyl, ethyl, amido (CONH_2), aminomethyl, methoxy and ethoxy.

11. (amended) A compound according to claim 1 wherein R_2 is selected from one of the formula (A') to (H'):

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wherein X₄ is O or S, R₁₃ is selected from hydrogen, fluoro, [except for (C')] chloro or methyl and R₁₄ is selected from hydrogen, methyl, ethyl, fluoro, chloro, and methoxy and
 5 R₁₅ is selected from hydrogen, methyl, fluoro, chloro and amino.

12. (amended) A compound according to claim 11, wherein R₂ is 4-chlorophenyl, 4-methoxyphenyl, 3-amino-4-chlorophenyl,
 10 indol-2-yl, 5-chloroindol-2-yl, indol-6-yl, 3-chloroindol-6-yl or 3-methylindol-6-yl.

13. (amended) A compound according to claim 1 wherein -X-X- is -CONH-.

- 10 -

14. (amended) A compound according to any one of claims 1 to 13, 15 to 16 and 19 to 22 wherein Y is CH.

15. (amended) A compound according to claim 1 wherein Cy is an optionally R_{3a} substituted: phenyl, pyridyl, thienyl, thiazolyl, naphthyl, piperidinyl, furanyl, pyrrolyl, isoxazolyl, isothiazolyl, pyrazolyl, oxazolyl, imidazolyl, 1,2,4-thiadiazolyl, 1,3,4-thiadiazolyl, pyrimidinyl, pyridazinyl, quinolyl, isoquinolyl, benzofuryl, benzothienyl or cycloalkyl group, or a phenyl group substituted by R_{3i}X_i in which X_i is a bond, O, NH or CH₂ and R_{3i} is phenyl, pyridyl or pyrimidyl optionally substituted by R_{3a}.

16. (amended) A compound according to claim 2 wherein Cy is an optionally R_{3a} substituted: phenyl, pyridyl, thienyl, thiazolyl, naphthyl, piperidinyl or cycloalkyl group.

17. (cancelled on national phase entry)

18. (cancelled on national phase entry)

19. (amended) A compound according to claim 15 wherein R_{3a} is selected from hydrogen, hydroxyl, methoxy, ethoxy, methyl, ethyl, methylaminomethyl, dimethylaminomethyl, hydroxymethyl, carboxy, methoxymethyl, methoxycarbonyl, ethoxycarbonyl, methylaminocarbonyl, dimethylamino-carbonyl, aminomethyl, CONH₂, CH₂CONH₂, acetyl amino, methoxycarbonylamino, ethoxycarbonylamino, t-butoxycarbonylamino, amino, fluoro, chloro, bromo, cyano, nitro, thiol, methylthio, methylsulphonyl, ethylsulphonyl, methylsulphenyl, methylsulphonylamido, ethylsulphonylamido, methylaminosulphonyl, ethylaminosulphonyl, aminosulphonyl, trifluoromethoxy, trifluoromethyl, bromo, -OCH₂O- (which is bonded to two adjacent ring atoms in Cy) and -C(X³)N(R¹¹)R¹² (wherein X³ is O or S and R¹¹ and R¹² are independently selected from hydrogen, methyl or ethyl or together with the nitrogen atom to which they are attached form a pyrrolidin-1-yl, piperidin-1-yl or morpholino group).

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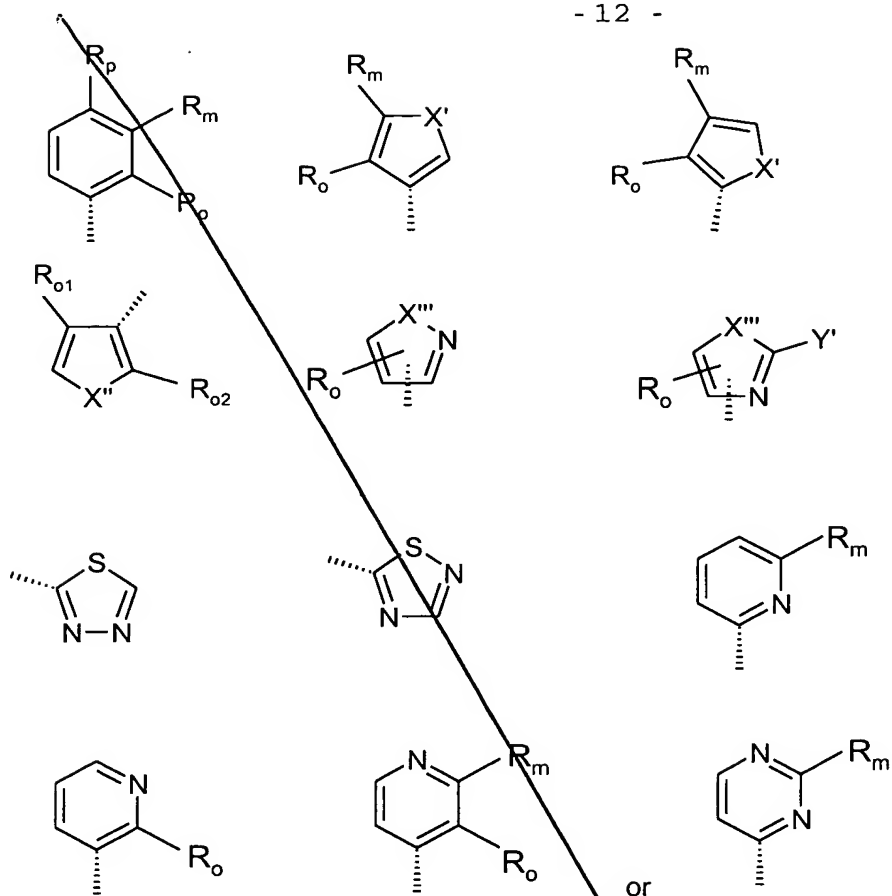
20. (amended) A compound according to claim 16 wherein R_{3a} is selected from hydrogen, hydroxyl, methoxy, ethoxy, methyl, ethyl, methylaminomethyl, dimethylaminomethyl, hydroxymethyl, 5 carboxy, methoxymethyl, methoxycarbonyl, ethoxycarbonyl, methylaminocarbonyl, dimethylamino-carbonyl, aminomethyl, CONH₂, CH₂CONH₂, acetyl amino, methoxycarbonylamino, ethoxycarbonylamino, t-butoxycarbonylamino, amino, fluoro, chloro, cyano, nitro, thiol, methylthio, methylsulphonyl, 10 ethylsulphonyl, methylsulphenyl, methylsulphonylamido, ethylsulphonylamido, methylaminosulphonyl, ethylaminosulphonyl, aminosulphonyl, trifluoromethoxy and trifluoromethyl.

15 21. (amended) A compound according to claim 1 wherein Cy is selected from:

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- 12 -



wherein:

X' is selected from O, S and NMe;

5 X'' is selected from O and S;

X''' is selected from O, S, NH and NMe;

Y' is selected from hydrogen, amino and methyl;

10 R_o is selected from hydrogen, methyl, fluoro, chloro, trifluoromethyl, methoxy, methylthio, methylsulphinyl and methylsulphonyl;

R_m is selected from hydrogen, methyl, fluoro, chloro, trifluoromethyl, methoxy, methylthio, methylsulphinyl, methylsulphonyl, carboxy, methoxycarbonyl and a group of the formula $-C(X^3)N(R^{11})R^{12}$ (wherein X^3 is O or S and R^{11} and R^{12} are independently selected from hydrogen, methyl or ethyl or together with the nitrogen atom to which they are attached form a pyrrolidin-1-yl, piperidin-1-yl or morpholino group);

R_p is selected from hydrogen and fluoro; or

R_o and R_m or R_m and R_p form an $-OCH_2O-$ group; or

20 R_o and R_m together with the ring to which they are attached

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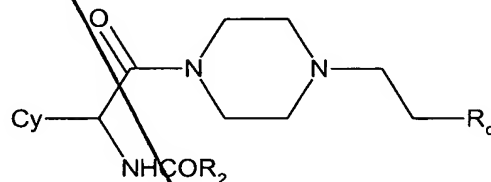
form a 5 or 6 membered aryl or heteroaryl ring (wherein the heteroaryl ring contains 1 or 2 heteroatoms selected from nitrogen, oxygen and sulfur);

one of R_{O1} and R_{O2} is hydrogen and the other is R_O ;

5

22. (amended) A compound according to claim 1 wherein Cy is selected from phenyl, 2-chlorophenyl, 2-methoxyphenyl, 4-carbamoylphenyl, pyrid-2-yl, pyrid-4-yl, thien-2-yl, thien-3-yl, furan-2-yl, furan-3-yl, imidazol-2-yl, thiazol-2-yl, 10 thiazol-4-yl, thiazol-5-yl and quinolin-4-yl.

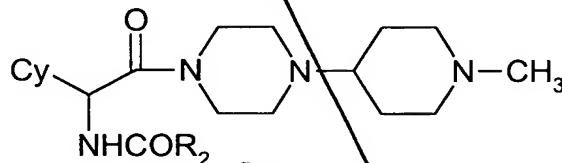
23. (amended) A compound of the formula:



wherein Cy, R_2 and R_C are as defined in claim 1.

15

24. (amended) A compound of the formula:



wherein Cy and R_2 are as defined in claim 1.

20

25. (amended) A compound as claimed in Claim 14, in which the alpha atom in Y is carbon and has the conformation that would result from construction from a D- α -aminoacid $NH_2-CR_{1b}(Cy)-COOH$ where the NH_2 represents part of X-X.

25

26. A compound as claimed in Claim 1, which is selected from:
 1-(Indole-6-carbonyl-D-phenylglycinyI)-4-[2-(4-pyridinyl)-ethyl]piperazine;
 1-(3-Chloroindole-6-carbonyl-D-phenylglycinyI)-
 30 4-[2-(4-pyridinyl)ethyl]piperazine;
 1-(4-Methoxybenzoyl-D-phenylglycinyI)-4-(1-methylpiperidin-4-

- 14 -

yl)piperazine;

1-(Indole-6-carbonyl-D-phenylglyciny1)-4-(1-methylpiperidin-4-yl)piperazine;

1-(4-Methoxybenzoyl-D-(2-chlorophenyl)glyciny1)-4-(1-methyl-
5 piperidin-4-yl)piperazine;1-(Indole-6-carbonyl-D-(2-chlorophenyl)glyciny1)-4-(1-methyl-
piperidin-4-yl)piperazine; and1-(4-Methoxybenzoyl-D-(2-trifluoromethylphenyl)glyciny1)-4-(1-
methylpiperidin-4-yl)piperazine;

10 and physiologically-tolerable salts thereof.

27. (amended) A pharmaceutical composition, which comprises a
compound as claimed in Claim 1 together with at least one
pharmaceutically acceptable carrier or excipient.

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28. (cancelled on national phase entry)

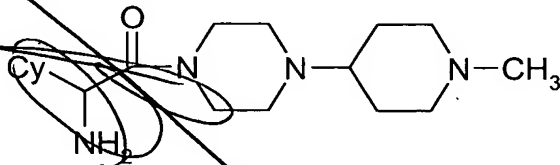
29. (cancelled on national phase entry)

20 30. A method of treatment of a human or non-human animal body
to combat a thrombotic disorder, which comprises administering
to said body an effective amount of a compound as claimed in
claim 1.

25 31. (cancelled on national phase entry)

32. (cancelled on national phase entry)

33. (amended) A compound of the formula



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in which Cy is as defined in Claim 1, or a salt thereof.

34. (new) 1-(Indole-6-carbonyl-D-phenylglyciny1)-4-(1-
methylpiperidin-4-yl)piperazine; or a physiologically-
35 tolerable salt thereof.

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35. (new) A pharmaceutical composition, which comprises a compound as claimed in Claim 34 together with at least one pharmaceutically acceptable carrier or excipient.

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36. (new) A method of treatment of a human or non-human animal body to combat a thrombotic disorder, which comprises administering to said body an effective amount of a compound as claimed in claim 34.

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